

## REMARKS

With the addition of claims 44-51, claims 1-3, 5-51 are pending.

The amendments to claims 3, 6, 9, 10, 12, 13, 26-28, 31 are editorial and would not narrow the scope of the amended claim recitations.

Claims 20, 21, 22, 25 and 32 have been amended by making them independent of the rejected base claims.

Support for the insertion of "contains less than about 5% wt of another famciclovir crystalline form" in claim 14, and the addition of claims 45-51, can be found in the specification at page 3, lines 20-24, and page 7, lines 15-16, and claim 41 as filed.

Support for the amendments to claim 36 can be found in the specification at page 5, lines 13-16 and page 12, lines 29-30.

Support for new claim 44 can be found in the specification at page 7, lines 19-21 and page 8, lines 6-9.

### Claim Objections

Claims 20-29 and 32 were objected to as dependent on a rejected base claim, but were held to contain allowable subject matter. Claims 20-29 and 32 have been made independent of any rejected base claim. Allowance of claims 20-29 and 32 is requested.

### Claim Rejection -- 35 U.S.C. 112, Second Paragraph

Applicants respectfully traverse the indefiniteness rejection of claim 5. The Office Action asserts that claim 5 was indefinite because the "claim limitation in the claim now is already required by claim 1." Applicants respectfully disagree. Claim 5 recites "wherein the crystalline solid famciclovir contains less than about 5% wt of **form II**", while claim 1 recites "wherein the crystalline solid famciclovir contains less than about 5% wt of **another famciclovir crystalline form**" (emphasis added). By referring to form II, the recitation in claim 5 is not the same as the claim limitation in claim 1.

Withdrawal of the indefiniteness rejection is requested.

### Claim Rejections -- 35 U.S.C. 112, First Paragraph

Applicants respectfully traverse the rejection of claims 11-17, 33, 34, 36 and 41-43 as failing to comply with the written description requirement. The specification discloses that methanol or ethanol solvate of famciclovir are characterized by PXRD peaks at  $6.6$  and  $13.0 \pm 0.2$  deg.  $2\theta$ . Claim 11 has been amended to be directed to the methanol solvate in order to

advance prosecution. Withdrawal of the rejection of claims 11-17, 33, 34, 36 and 41-43 is requested.

Applicants also respectfully traverse the non-enablement rejection of claims 30 and 35. The Examiner rejected claims 30 and 35 on non-enablement grounds because some solvents are used in the processes of both claims. Applicants respectfully note that, in the process of claim 35, one or more mixtures of the recited organic solvent and water are used, which would cover the situation in which the recited organic solvents contain low levels of water. As a result, the recitations “ethanol/water mixture, DMF/water mixture, DMA/water mixture, acetonitrile/water mixture, methanol/water mixture, tetrahydrofuran/water mixture, and/or isopropyl alcohol/water mixture” cover, among other situations, the situation in which a solution of famciclovir in ethanol, DMF, DMA, acetonitrile, methanol, tetrahydrofuran and/or isopropyl alcohol containing a little of water is used. With the presence of water in the famciclovir solution, the process of claim 35 can produce famciclovir monohydrate. The organic solvents recited in claim 30 can produce crystalline famciclovir Form I. There is no overlap of the solvents used in the processes of claims 30 and 35. Claims 30 and 35 do not contradict each other. Thus, applicants respectfully contend that claims 30 and 35 are both enabled.

Page 8 of the Office Action wants the applicants to clarify what produces famciclovir monohydrate and what produces a mixture of famciclovir Forms I and II (both Forms I and II are anhydrous according to page 6, lines 19-20, of the specification). It appears that what prompted the Office Action to seek clarification was the Examiner’s observation that Example 11 in pages 13-14 disclosed an experiment in which using isopropyl alcohol in a process resulted in a mixture of famciclovir monohydrate and famciclovir Form I, while runs 9-11 of Table 1 in page 11 used isopropyl alcohol and resulted in a mixture of famciclovir Forms I and II. Applicants would like to direct the Examiner’s attention to Table 1 which states that runs 9-11 used Method B, which is disclosed in page 10, lines 18-19, in that the famciclovir crystals obtained were dried. The drying of the famciclovir crystals would remove water from famciclovir monohydrate resulting in anhydrous famciclovir. Thus, there is no inconsistency between Example 11 and runs 9-11 of Table 1.

Applicants also respectfully traverse the non-enablement rejection of claim 35. The Office Action alleges that the preparation of the monohydrate was enabled only with the use of DMF/water presumably because of what Example 10 shows, but not enabled for the use of non-aqueous solvents (see the last two lines of page 8 of the Office Action). The Office Action states using non-aqueous solvents in the process of claim 35 cannot make the hydrate without a source of water. Claim 35 has been amended so that it recites “ethanol/water mixture, DMF/water mixture, DMA/water mixture, acetonitrile/water mixture, methanol/water mixture, tetrahydrofuran/water mixture, and/or isopropyl alcohol/water mixture.” There is a source of

water. Claim 35 covers, among other situations, the situation in which a solution of famciclovir in ethanol, DMF, DMA, acetonitrile, methanol, tetrahydrofuran and/or isopropyl alcohol containing a little of water is used. Withdrawal of the nonenablement rejection of claim 35 is requested.

The Office Action alleges that claim 35 was not enabled when the recited organic solvent/water mixtures used was not DMF/water mixture as shown in Example 10. For the non-enablement rejection of claim 35, the Examiner relied on Brand; *Tetrahedron* (1999) 55: 5239-5252, in which page 5251 reports that crystallization from aqueous acetone gave famciclovir. The Examiner asserted that because Brand reported the preparation of famciclovir, not famciclovir monohydrate, using aqueous acetone, the use of ethanol/water mixture, DMA/water mixture, acetonitrile/water mixture, methanol/water mixture, tetrahydrofuran/water mixture, or isopropyl alcohol/water mixture in the process of claim 35 was not enabled. Applicants respectfully disagree. Just because Brand was silent on famciclovir monohydrate does not mean that no famciclovir monohydrate was prepared by Brand when he used aqueous acetone. Especially because Brand used only  $^1\text{H}$ -NMR and  $^{13}\text{C}$ -NMR performed in solution, the NMR techniques used by Brand would not be expected to differentiate famciclovir from famciclovir monohydrate. One skilled in the art would recognize that one may need to use  $^{13}\text{C}$ -solid-state NMR, preferably coupled with the use of high power proton decoupling, magic angle spinning and cross-polarization, to differentiate a crystalline substance from its hydrate. Thus, applicants submit that the results of Brand do not rule out the formation of famciclovir monohydrate in the experiment using aqueous acetone. Since the use of ethanol/water mixture, DMA/water mixture, acetonitrile/water mixture, methanol/water mixture, tetrahydrofuran/water mixture, and/or isopropyl alcohol/water mixture in the process of claim 35 would provide water molecules in the crystallization reaction of famciclovir, there is not technical reason to doubt the applicants' disclosure that the process would result in famciclovir monohydrate. Withdrawal of the non-enablement rejection of claim 35 is requested.

Regarding the Examiner's comments concerning Example 11 presented in page 9 of the Office Action, applicants agree with the Examiner's observation that the suspension of famciclovir in isopropyl alcohol used in Example 11 contained some water, so that famciclovir monohydrate was produced in Example 11. The Examiner queried why moisture did not happen in runs 9-12 of Example 1, in which the use of isopropyl alcohol did not result in famciclovir monohydrate. As explained above, runs 9-11 of Example 1 were different from Example 11 in that, among other differences, runs 9-11 of Example 1 dried the famciclovir crystals so that any water molecules in the crystals would be driven off resulting in anhydrous famciclovir solid. In contrast, Example 11 did not dry the crystals of a mixture of famciclovir monohydrate and

crystalline solid famciclovir Form I. That explains why runs 9-12 of Example 1 should not be compared with Example 11.

#### Claim Rejections -- 35 U.S.C. §102

(A) Applicants respectfully traverse the anticipatory rejection of claim 35 over Harnden 1990 (*Nucleosides & Nucleotides* (1990) 9:499-513). The Examiner rejected claim 35 because tiny traces of methanol would be expected to be present in the crystallization step of Harnden 1990 and because claim 35 recites “methanol/water mixture” reads on, for example, one part per billion of methanol in water, without any limits on the ratio. Harnden 1990 prepared famciclovir by hydrogenation of 9-[4-acetoxy-3-(acetoxymethyl)butyl]-2-amino-6-chloropurine according to the procedure disclosed in Harnden 1989 (*J. Med. Chem.* (1989) 32: 1738-1743), followed by crystallization from water to yield famciclovir monohydrate (p. 501, first sentence of the first full paragraph). The Examiner relied on page 1741 of Harnden 1989 for the alleged disclosure that the famciclovir used in Harnden 1990 contained traces of methanol.

One of the reasons why the anticipatory rejection of claim 35 should be withdrawn is that the rejection over Harnden 1990 is an improper anticipatory rejection since the rejection actually relies on the disclosures of two references, Harnden 1990 in view of Harnden 1989. A prior art reference anticipates a claimed invention if it describes, expressly or inherently, all the limitations of the claim. *See EMI Group North America, Inc. v. Cypress Semiconductor Corporation*, 268 F.3d 1342, 1350 (Fed. Cir. 2001) (citing *Kalman v. Kimberly-Clark Corp.*, 713 F.2d 760, 771 (Fed. Cir. 1983); *Hughes Aircraft Co. v. United States*, 15 Cl. Ct. 267, 271 (1988) (“The mere fact that a prior art reference failed to mention something that undeniably existed is of no consequence, for the element must have been there.”), *dismissed in part, aff’d in part, without op.*, 862 F.2d 320 (Fed. Cir. 1988); *Verdegaal Bros., Inc. v. Union Oil Co.*, 814 F.2d 628, 633 (Fed. Cir. 1987) (rejecting an argument that prior use of process did not anticipate patent because prior inventor did not explicitly recognize additional properties); *In re King*, 801 F.2d 1324, 1326 (Fed. Cir. 1986). A claim limitation is inherently described in a prior art reference if the claimed feature that is missing from the express disclosure necessarily flows from, or is a natural result of, what is disclosed in the reference. *In re Oelrich*, 666 F.2d 578, 581 (CCPA 1981). In the instant case, Harnden 1990 does not describe, expressly and inherently, all the elements of claim 35. Harnden 1990 does not expressly disclose how the crude famciclovir of Harnden 1989 was prepared. One skilled in the art reading Harnden 1990 would not necessarily know how the crude famciclovir of Harnden 1989 was prepared. The crude famciclovir of Harnden 1989 is also not inherently disclosed in Harnden 1990 because the crude famciclovir as prepared by the process disclosed in Harnden 1989 does not naturally flow from the disclosure in Harnden 1990. Harnden 1989 is not cited to (a) prove that Harnden 1990

contains an enabled disclosure, (b) explain the meaning of a term used in Harnden 1990, or (c) show that a characteristic not disclosed in Harnden 1990 is inherent. *See* MPEP 2131.01. Because the anticipatory rejection of claim 35 was based on a prior reference which does not disclose each and every element of claim 35, withdrawal of the anticipatory rejection is requested.

Another reason why the anticipatory rejection of claim 35 over Harnden 1990 is that the Examiner misinterpreted the disclosures of Harnden 1989. The Examiner asserted that Harnden 1989 teaches famciclovir containing traces of methanol. Applicants respectfully disagree. Near the bottom of page 1741, right column, Harnden 1989 discloses a process of preparing famciclovir by

(a) hydrogenating a suspension of 9-[4-acetoxy-3-(acetoxymethyl)butyl]-2-amino-6-chloropurine and palladium on charcoal in methanol containing ammonium formate under reflux for 30 min.;

(b) cooling and filtering;

(c) removing the solvent;

(d) taking the residue up in water to form a solution;

(e) extracting the solution twice with chloroform;

(f) combining the organic layers and drying over  $\text{MgSO}_4$ ; and then

(g) removing the solvent to afford famciclovir.

The Office Action states that the two-time extraction with chloroform was immaterial because chloroform extraction would be expected to bring with it some of the methanol. Applicants respectfully disagree. Attached is a copy of an entry on Solvent taken from Wikipedia at <http://en.wikipedia.org/wiki/Solvent>, which states that a rule of thumb is “like dissolves like” and the polarity of a solvent determines with what other solvents it is miscible with. The table in the Wikipedia entry shows that chloroform, a non-polar solvent, has a dielectric constant of 4.8, while methanol, a polar protic solvent, has a much higher dielectric constant of 33. Thus, applicants contend that the two-times extraction with chloroform would not be expected to bring with it methanol. Furthermore, applicants maintain that, in the procedure of Harnden 1989, whatever little, if any, methanol that might have remained before step (f) would have been removed in step (g). Thus the crude famciclovir obtained in step (g) would not contain any methanol. This is another reason for requesting withdrawal of the anticipatory rejection of claim 35.

(B) Applicants also respectfully traverse the anticipatory rejections of claims 1-3, 5-10, 18, 19, 31 and 37-43 over Harnden 1989 (*J. Med. Chem.* (1989) 32: 1738-1743); US 5,017,701;

US 5,066,805; US 5,138,057; US 6,846,927; US 6,342,603; Freer (*Tetrahedron* (2000) 56:4589-4595); US 6,437,125 and WO 2000/06573.

The Examiner relied upon

Harnden 1989 for disclosing crystallization from ethyl acetate/hexane;

US 5,017,701 or US 6,342,603 for disclosing crystallization from n-butanol;

US 5,066,805 for disclosing evaporation from chloroform/methanol;

US 5,138,057 for disclosing crystallization from ethyl acetate/diethyl ether or from n-butanol;

US 6,846,927 for disclosing recrystallization from n-butanol and then reslurrying in n-heptane;

Freer or US 6,437,125 for disclosing crystallization from hot isopropanol; and

WO 2000/06573 for disclosing triturating with diethyl ether.

The differences between the cited prior art and the claimed invention presented in the Response to the previous Office Action filed on February 28, 2006 are incorporated by reference. In particular, applicants note that, contrary to the allegation by the Office Action, US 5,138,057 does not disclose crystallization of famciclovir from ethyl acetate/diethyl ether. Actually, column 8, lines 10-12, of US 5,138,057 discloses crystallization of a 6,8-dichloro intermediate of famciclovir, not famciclovir itself, from ethyl acetate/diethyl ether.

The Office Action maintains that applicants have the burden to show, with data, that the crystalline famciclovir prepared in the cited prior art references was not the crystalline famciclovir Form I or Form II according to the instant claims because the cited references were silent merely on the property of famciclovir. Applicants respectfully disagree. The Office Action cites the MPEP for stating that something which is old does not become patentable upon the discovery of a new property. Applicants note that the crystalline form is not a "property" of famciclovir. Crystalline famciclovir Form I and Form II are two novel forms of famciclovir. Thus, crystalline famciclovir Form I and Form II are not properties of an old compound. Crystalline famciclovir Form I and Form II are two different physical entities, and not merely "characteristic" which the prior art is silent on. There is no evidence that the cited prior art teaches crystalline famciclovir Form I and Form II. This is one of the reasons why the anticipatory rejections should be withdrawn.

Regarding the process claim 18, the Office Action asserts that the prior art that discloses the use of diethyl ether in crystallization anticipates claim 18. However, as pointed out above, US 5,138,057 discloses crystallization of a 6,8-dichloro precursor of famciclovir, not famciclovir itself, from ethyl acetate/diethyl ether. Concerning the alternative trituration of anhydrous famciclovir in isopropyl alcohol in the process of claim 18, Freer does not anticipate because

Freer merely discloses recrystallizing famciclovir from hot isopropyl alcohol, filtering the product and washing with isopropyl alcohol. The washing with isopropyl alcohol is not trituration because it was not mixing a solid with a liquid. When a filtered product is washed with a liquid, one skilled in the art usually would merely pour the liquid through the filter paper on which the product has been collected. Similarly, the cited prior art does not teach the processes of claims 30 and 31. Thus, withdrawal of the anticipatory rejections of claims 18, 30 and 31 is requested.

Regarding the anticipatory rejection of method claim 43, because the pharmaceutical composition of any one of claims 37-42 is novel due to the novelty of Form I and Form II discussed above, withdrawal of the anticipatory rejection of claim 43 is requested.

Withdrawal of all the anticipatory rejections is requested.

Page 3 of the Office Action also states that Brand (*Tetrahedron* 55 (1999) 5239-5252) discloses in page 5151 crystallization from aqueous acetone. Page 9, lines 5-6, of the Office Action states that: "No claims are anticipated over Brand." Applicants, as a result, have treated the statement in page 3 of the Office Action as merely a comment, not a rejection or objection. The Brand reference has been dealt with by applicants in the above non-enablement rejection.

In the event that the filing of this paper is deemed not timely, applicants petition for an appropriate extension of time. The petition fee and any other fees that may be required in relation to this paper can be charged to Deposit Account No. 11-0600 referencing Attorney Docket No. 01662/60903.

Respectfully submitted,

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Enclosure: Entry on Solvent taken from Wikipedia at <http://en.wikipedia.org/wiki/Solvent>

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# Solvent

From Wikipedia, the free encyclopedia

A **solvent** is a fluid phase (liquid, gas, or plasma) that dissolves a solid, liquid, or gaseous solute, resulting in a solution. The most common solvent in everyday life is water. The term **organic solvent** refers to most other solvents that are organic compounds and contain carbon atoms. Solvents usually have a low boiling point and evaporate easily or can be removed by distillation, thereby leaving the dissolved substance behind. Solvents should therefore not react chemically with the dissolved compounds — they have to be inert. Solvents can also be used to extract soluble compounds from a mixture, the most common example is the brewing of coffee or tea with hot water. Solvents are usually clear and colorless liquids and most of them have a characteristic odor. The concentration of a solution is the amount of compound that is dissolved in a certain volume of solvent. The **solubility** is the maximal amount of compound that is soluble in a certain volume of solvent at a specified temperature.

Common uses for organic solvents are in dry cleaning (e.g. tetrachloroethylene), as paint thinners (e.g. toluene, turpentine), as nail polish removers and glue solvents (acetone, methyl acetate, ethyl acetate), in spot removers (e.g. hexane, petrol ether), in detergents (citrus terpenes), in perfumes (ethanol), and in chemical syntheses.

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## Polarity, solubility, and miscibility

Solvents and solutes can be broadly classified into *polar* (hydrophilic) and *non-polar* (lipophilic). The polarity can be measured as the dielectric constant or the dipole moment of a compound. The polarity of a solvent determines what type of compounds it is able to dissolve and with what other solvents or liquid compounds it is miscible. As a rule of thumb, polar solvents dissolve polar compounds best and non-polar solvents dissolve non-polar compounds best: "like dissolves like". Strongly polar compounds like inorganic salts (e.g. table salt) or sugars (e.g. sucrose) dissolve only in very polar solvents like water, while strongly non-polar compounds like oils or waxes dissolve only in very non-polar organic solvents like hexane. Similarly, water and hexane (or vinegar and salad oil) are not miscible with each other and will quickly separate into two layers even after being shaken well.

## Protic and aprotic solvents

Polar solvents can be further subdivided into polar protic solvents and polar aprotic solvents. Water (H-O-H), ethanol (CH<sub>3</sub>-CH<sub>2</sub>-OH), or acetic acid (CH<sub>3</sub>-C(=O)OH) are representative polar protic solvents. A polar aprotic solvent is acetone (CH<sub>3</sub>-C(=O)-CH<sub>3</sub>). In chemical reactions the use of polar protic solvents favors the S<sub>N</sub>1 reaction mechanism, while polar aprotic solvents favor the S<sub>N</sub>2 reaction mechanism.

## Boiling point

Another important property of solvents is boiling point. This also determines the speed of evaporation. Small amounts of low-boiling solvents like diethyl ether, dichloromethane, or acetone will evaporate in seconds at room temperature, while high-boiling solvents like water or dimethyl sulfoxide need higher temperatures, an air flow, or the application of vacuum for fast evaporation.



Water is a strange exception in this sense, because most solvents of the same size tend to evaporate in very low temperatures. The exception is caused by cohesion i.e., at high temperatures, several water molecules will group together and act as a larger molecule - and evaporate.

## Density

Most organic solvents have a lower density than water, which means they are lighter and will form a separate layer on top of water. An important exception: many halogenated solvents like dichloromethane or chloroform will sink to the bottom of a container, leaving water as the top layer. This is important to remember when partitioning compounds between solvents and water in a separatory funnel during chemical syntheses.

## Chemical interactions

A solvent will create various weak chemical interactions with the solute to solubilize the solute. The most usual of these interactions are the relatively weak van der Waals interactions (induced dipole interactions), the stronger dipole-dipole interactions, and the even stronger hydrogen bonds (interaction between O-H or N-H hydrogens with O or N atoms).

## Health and Safety

Most organic solvents are flammable or highly flammable, depending on their volatility. Exceptions are some chlorinated solvents like dichloromethane and chloroform. Mixtures of solvent vapors and air can explode. Solvent vapors are heavier than air, they will sink to the bottom and can travel large distances nearly undiluted. Solvent vapors can also form in supposedly empty drums and cans, posing a flash fire hazard; hence empty containers of volatile solvents should be stored open and upside down.

Ethers like diethyl ether and tetrahydrofuran (THF) can form highly explosive organic peroxides upon exposure to oxygen and light. These peroxides will concentrate during distillation due to their higher boiling point. Ethers have to be stored in the dark in closed canisters in the presence of stabilizers like BHT or over sodium hydroxide.

Many solvents can lead to a sudden loss of consciousness if inhaled in larger amounts. Solvents like diethyl ether and chloroform have been used in medicine as anesthetics and narcotics for a long time. Ethanol is a widely used and abused psychoactive drug. Diethyl ether, chloroform, and many other solvents (e.g. from gasoline or glues) are used recreationally in glue sniffing, often with harmful long term health effects like neurotoxicity or cancer. A major pathway to induce health effects arises from spills or leaks of solvents that reach the underlying soil. Since solvents readily migrate substantial distances, the creation of widespread soil contamination is not uncommon; there may be about 5000 sites worldwide that have major subsurface solvent contamination; this is particularly a health risk if aquifers are affected.

Some solvents including chloroform and benzene (an ingredient of gasoline) are carcinogenic. Many others can damage internal organs like the liver, the kidneys, or the brain. Methanol can cause internal damage to the eyes, including permanent blindness.

### General precautions

- Avoid the generation of solvent vapors by working in a fume hood, local exhaust ventilation (LEV) or a well ventilated area
- Keep the storage containers tightly closed.
- Never use open flames near flammable solvents, use electrical heating instead.
- Never flush flammable solvents down the drain to avoid explosions and fires.
- Avoid the inhalation of solvent vapors.
- Avoid contact of the solvent with the skin — many solvents are easily absorbed through the skin. They also tend to dry the skin and thus cause sores and wounds.

## Properties table of common solvents

The solvents are grouped into non-polar, polar aprotic, and polar protic solvents and ordered by increasing polarity. The polarity is

given as the dielectric constant. The density of nonpolar solvents that are heavier than water is bolded.

Solvent	Chemical Formula	Boiling point	Dielectric constant?? (use the tables linked at the bottom to be safe)	Density
<b>Non-Polar Solvents</b>				
Hexane	$\text{CH}_3\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{-CH}_3$	69 °C	2.0	0.655 g/ml
Benzene	$\text{C}_6\text{H}_6$	80 °C	2.3	0.879 g/ml
Toluene	$\text{C}_6\text{H}_5\text{-CH}_3$	111 °C	2.4	0.867 g/ml
Diethyl ether	$\text{CH}_3\text{CH}_2\text{-O-CH}_2\text{-CH}_3$	35 °C	4.3	0.713 g/ml
Chloroform	$\text{CHCl}_3$	61 °C	4.8	<b>1.498 g/ml</b>
Ethyl acetate	$\text{CH}_3\text{-C(=O)-O-CH}_2\text{-CH}_3$	77 °C	6.0	0.894 g/ml
Dichloromethane	$\text{CH}_2\text{Cl}_2$	40 °C	9.1	<b>1.326 g/ml</b>
<b>Polar Aprotic Solvents</b>				
1,4-Dioxane	$\text{/-CH}_2\text{-CH}_2\text{-O-CH}_2\text{-CH}_2\text{-O-CH}_2\text{-CH}_2\text{-/}$	101 °C	2.3	1.033 g/ml
Tetrahydrofuran (THF)	$\text{/-CH}_2\text{-CH}_2\text{-O-CH}_2\text{-CH}_2\text{-/}$	66 °C	7.5	0.886 g/ml
Acetone	$\text{CH}_3\text{-C(=O)-CH}_3$	56 °C	21	0.786 g/ml
Acetonitrile (MeCN)	$\text{CH}_3\text{-C}\equiv\text{N}$	82 °C	37	0.786 g/ml
Dimethylformamide (DMF)	$\text{H-C(=O)N(CH}_3)_2$	153 °C	38	0.944 g/ml
Dimethyl sulfoxide (DMSO)	$\text{CH}_3\text{-S(=O)-CH}_3$	189 °C	47	1.092 g/ml
<b>Polar Protic Solvents</b>				
Acetic acid	$\text{CH}_3\text{-C(=O)OH}$	118 °C	6.2	1.049 g/ml
<i>n</i> -Butanol	$\text{CH}_3\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{-OH}$	118 °C	18	0.810 g/ml
Isopropanol	$\text{CH}_3\text{-CH(OH)-CH}_3$	82 °C	18	0.785 g/ml
<i>n</i> -Propanol	$\text{CH}_3\text{-CH}_2\text{-CH}_2\text{-OH}$	97 °C	20	0.803 g/ml
Ethanol		79 °C	24	0.789 g/ml

	$\text{CH}_3\text{-CH}_2\text{-OH}$			g/ml
Methanol	$\text{CH}_3\text{-OH}$	65 °C	33	0.791 g/ml
Formic acid	$\text{H-C(=O)OH}$	100 °C	58	1.21 g/ml
Water	$\text{H-O-H}$	100 °C	80	0.998 g/ml

## See also

- LogP or partition coefficient is a measure of differential solubility of a compound in two solvents
- Solvent systems exist outside the realm of ordinary organic solvents: Supercritical fluids, ionic liquids and deep eutectic solvents.
- Water pollution

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## External links

- Table (<http://www.spekanalytical.co.uk/products/Tips/bps.html>) Properties of common organic solvents
- Table and text ([http://www.usm.maine.edu/~newton/Chy251\\_253/Lectures/Solvents/Solvents.html](http://www.usm.maine.edu/~newton/Chy251_253/Lectures/Solvents/Solvents.html)) O-Chem Lecture
- Tables (<http://virtual.yosemite.cc.ca.us/smurov/orgsoltab.htm>) Properties and toxicities of organic solvents
- Miscibility Table (<http://www.phenomenex.com/phen/Doc/z366.pdf>) Phenomex Solvent Miscibility Table (includes Polarity Index)
- Miscibility Table (<http://www.gls.co.jp/english/pdf/83.PDF>) GLS Solvent Miscibility Table (includes Dielectric Constant)

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